Amendments to the Drawings:

The attached new replacement sheet of drawing includes changes to Figure 8 and replaces the original sheet including Figure 8, and also replaces a prior replacement sheet submitted on February 12, 2008.

The Office objected to the prior replacement Figure 8 because the numbers indicating positions of the nucleic acids have been changed as compared to original Figure 8. Applicants submit that those changes were typographical errors. Thus, a new replacement figure is submitted herewith to match the original Fig. 8, and does not introduce any substantive changes.

Attachments following last page of this Amendment:

Replacement Sheet (1 page)

REMARKS

Upon entry of the proposed amendments, claims 7-10, 13-15, 36, 39, 40, and 44-52 would be pending. Claims 45-50 have been withdrawn, and claims 1-6, 11, 12, 16-35, and 38 have been previously canceled. Applicants have proposed to amend claims 7 and 8, cancel claims 37 and 41-43, and add new claims 51 and 52. Support for the proposed amendments to claims 7 and 8, and new claims 51 and 52 can be found throughout the specification, for example, at page 20, lines 30-31; page 21, line 25; Tables 1and 2; and original claim 4. Applicants submit that these proposed amendments would place the claims into condition for allowance, would introduce no new matter, would raise no new issues or require any additional searching, and would at least present the rejected claims in better form for consideration on appeal, and should therefore be entered after the final rejection under 37 C.F.R. § 1.116. Applicants are filing a Notice of Appeal herewith.

Telephone Interview with the Examiner

Applicants thank Examiner Lucas for the telephone interview with applicants' representative on October 16, 2008, regarding the Information Disclosure Statement (IDS) filed on September 8, 2004. Examiner Lucas indicated that he will not consider those references cited in that IDS unless applicants file a new IDS accompanied by the statement under 37 C.F.R § 1.97(e), or a new IDS with a Request for Continued Examination, since the September 8, 2004 IDS was defective. Applicants' representative pointed out that the defect of the September 8, 2004 IDS was remedied by the February 12, 2008 submission of the omitted copies of the references cited in that IDS.

Information Disclosure Statement

The Office (Office Action at page 2) stated that later submission of copies of the references cited in the Information Disclosure Statement (IDS) filed on September 8, 2004 did not bring that IDS into compliance with the rules. The Office therefore did not consider these cited references. Applicants respectfully disagree.

The September 8, 2004 IDS was timely filed before the mailing of a first office action on the merits, as provided by 37 C.F.R § 1.97(b). Applicants inadvertently did not include copies of those cited references that are not U.S. patents or patent applications. After the Office pointed out this oversight in the first office action dated October 12, 2007, applicants submitted copies of those references on February 12, 2008, before mailing of a final office action.

MPEP 609.05(a) states:

> If an information disclosure statement does not comply with the requirements based on the time of filing of the IDS as discussed in MPEP § 609.04(b), including the requirements for fees and/or statement under 37 CFR 1.97(e), the IDS will be placed in the application file, but none of the information will be considered by the examiner. The examiner may use form paragraph 6.49 which is reproduced below to inform applicant that the information has not been considered. Applicant may then file a new information disclosure statement **or correct the deficiency in the previously filed IDS**, but the date that the new IDS **or correction** is filed will be the date of the IDS for purposes of determining compliance with the requirements based on the time of filing of the IDS (37 CFR 1.97) (emphasis added)

Thus, applicants can correct a defect in a previously filed IDS by submitting the missing material, and do not have to file a new IDS. The date, prior to mailing of a final office action, on which applicants submitted the omitted copies of the cited references serves as the basis for determining compliance with the requirement. As provided in 37 C.F.R. § 1.97(c), an IDS filed before mailing of a final office action shall be considered by the Office if accompanied by the fee set forth in 37 C.F.R. § 1.17(p). In the reply to the previous office action filed along with the copies of the cited references, applicants requested the Office to apply any other charges to Deposit Account No. 06-1050. Thus, applicants submit that the February 12, 2008 filing of the copies of the references cited on the September 8, 2004 IDS was in compliance with the rules.

Accordingly, applicants respectfully request that the Office charge the fee under 37 C.F.R. § 1.17(p) to Deposit Account No. 06-1050 if it has not done so already, consider those non-patent references disclosed in the September 8, 2004 IDS, and return a copy of initialed form 1449 to applicants.

Drawings

The Office (Office Action at page 2) objected to the replacement copy of Figure 8 submitted previously, because it "...has been modified such that the placement of the numbers relating to the positions of the provided sequence have been changed." Applicants submit that those changes were typographical errors. Thus, a new replacement figure is submitted herewith to match the original Fig. 8, and does not introduce any substantive changes.

Withdrawn rejections

Applicants note with appreciation that the Office has withdrawn a number of rejections under 35 U.S.C. § 112, 35 U.S.C. § 102, and 35 U.S.C. § 103.

35 U.S.C. § 112

The Office rejected claims 7-10, 13, 14, 15, 36, 37, 39, and 40-44 as allegedly failing to comply with the written description requirement. According to the Office Action (at pages 4-6):

> In the present case, the application identifies certain modified MLV envelope proteins which meet the structural and functional requirements of the claims. See e.g., page 20, lines 21-31 ... However, it is noted that the application teaches that not every nucleic acid that meets the structural requirements of the claims also meets the functional requirements ... In view of the uncertainty as to the operability of other undisclosed species, and the fact that the disclosed species relate to only a few potential positions and only two of the innumerable potential heterologous peptides, the disclosed species are not found to be sufficiently representative of the claimed genus as a whole.

Applicants do not necessarily agree. However, for the sole purpose of moving this application towards allowance, applicants have amended the claims to recite amino acid position 38 for inserting an RGD ligand or a gastrin releasing protein (GRP) ligand. The specification (see, e.g., Examples 3, 4 and 7) provides ample data showing that a retroviral particle comprising a chimeric retrovirus envelope protein with one of these ligands inserted at the recited position is capable of infecting human cells, but not mouse cells. Thus, the instant claims are adequately described. Applicants respectfully request reconsideration and withdrawal of this rejection.

35 U.S.C. § 103

The Office rejected claims 7-10, 13-15, 36, 37, and 39-44 as allegedly obvious over Kingsman (U.S. Pat. No.6,132,731) in view of Paul et al. (U.S. Pat. No. 5,736,387; "Paul") and Panda et al. (Virology, 2000, 273:90-100; "Panda"). Applicants do not agree, and traverse with respect to the presently amended claims.

According to the Office Action (at page 9), amino acid position 68 of the SU corresponds to a residue within a region (i.e., the second proline in site II) identified in Kingsman as a potential site for peptide insertion. However, there is nothing in Kingsman to suggest inserting a heterologous ligand at position 38 of the SU, as recited in the present claims.

The Office appeared to suggest that because a RGD ligand was known to bind to melanoma cells, a retroviral particle comprising a RGD ligand would inherently bind to such cells. However, as the Office acknowledged (Office Action at page 5) and discussed in Kingsman (see, e.g., column 2, lines 31-39 and column), not any heterologous ligand inserted at any position within a viral envelope protein would result in a functional retroviral particle capable of infecting human cells. Kingsman itself suggests that only certain regions are suitable for positioning a heterologous peptide for various reasons, and in fact, supposedly identified two such regions. Even so, Kingsman admits that one of the identified regions turned out to not to be suitable (see, e.g., column 8, lines 10-11 and column 11, lines 36-3). Thus, skilled practitioners would not have had a reasonable expectation of success that a ligand (e.g., a RGD ligand or a GRP ligand) inserted at position 38 of the SU of a MLV ecotropic envelope protein would create a functional retroviral particle capable of infecting human cells, and not mouse cells.

Neither Paul nor Panda remedies the deficiencies of Kingsman. The Office pointed to Paul and Panda apparently for suggesting that skilled practitioners would have known how to generate a retroviral particle not capable of infecting mouse cells. However, neither Paul nor Panda suggests inserting a heterologous ligand at the specific position recited in the claims. Thus, these two references would not have led skilled practitioners to applicants' claimed nucleic acid molecule, vector, or method of altering retroviral tropism of a retrovirus. As the two references do not suggest inserting a heterologous ligand at the recited position, skilled practitioners would not have been motivated to do so by reading Paul or Panda.

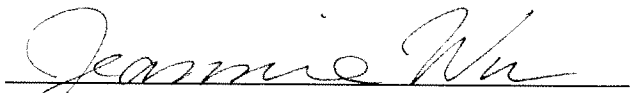
In view of the foregoing, applicants submit that the present claims are not obvious over Kingsman in view of Paul and Panda. Applicants respectfully request that the Office reconsider and withdrawal this rejection.

CONCLUSION

Applicants respectfully request that all claims be allowed. Applicants do not concede any positions of the Examiner that are not expressed above, nor do applicants concede that there are not other good reasons for patentability of the presented claims or other claims. The fees for a three-months extension and the Notice of Appeal in the amount of $825 are being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 07917-166US1.

Respectfully submitted,

Date: October 17, 2008



Jeannie Wu, Ph.D.
Reg. No. 56,265

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (877) 769-7945

22005592.doc